RECORDATI RARE DISEASES GROUP

IMPORTANT PRESCRIBING INFORMATION

March 8, 2022

Subject: Shortage of US-labeled TRANXENE T-TAB® Tablets (clorazepate dipotassium tablets, USP) 7.5 mg

Dear Health Care Provider,

Recordati Rare Diseases has determined there will be an inability to supply the market with TRANXENE T-TAB® Tablets (clorazepate dipotassium tablets, USP) 7.5 mg approved for use and distribution in the United States ("US-labeled TRANXENE"). The current available lot of Tranxene (20K08) has an expiration date of 7/31/22 and will be sold until 4/30/22. Recordati Rare Diseases is working to address this matter.

U.S. FDA-approved Indication

TRANXENE (clorazepate dipotassium) is a benzodiazepine. TRANXENE tablets are indicated for the management of anxiety disorders or for the short-term relief of the symptoms of anxiety. Anxiety or tension associated with the stress of everyday life usually does not require treatment with an anxiolytic.

TRANXENE tablets are indicated as adjunctive therapy in the management of partial seizures.

The effectiveness of TRANXENE tablets in long-term management of anxiety, that is, more than 4 months, has not been assessed by systematic clinical studies. Long-term studies in epileptic patients, however, have shown continued therapeutic activity. The physician should reassess periodically the usefulness of the drug for the individual patient.

TRANXENE tablets are indicated for the symptomatic relief of acute alcohol withdrawal.

For reporting of adverse events and more information

Any adverse effects or medication issues resulting from the use of this drug or quality issues should be reported to Recordati Rare Diseases Inc. at 1-888-575-8344 or to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax:

- Complete and submit the report **Online**: www.fda.gov/medwatch/report.htm
- **Regular mail or Fax**: Download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178.

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Important Safety Information

WARNING: RISKS FROM CONCOMINANT USE WITH OPIOIDS

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death (see WARNINGS, DRUG INTERACTIONS)

- Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioids alone. If a decision is made to prescribe TRANXENE concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation. In patients already receiving an opioid analgesic, prescribe a lower initial dose of TRANXENE than indicated in the absence of an opioid and titrate based on clinical response. If an opioid is initiated in a patient already taking TRANXENE, prescribe a lower initial dose of the opioid and titrate based upon clinical response.

Advise both patients and caregivers about the risks of respiratory depression and sedation when TRANXENE is used with opioids. Advise patients not to drive or operate heavy machinery until the effects of concomitant use with the opioid have been determined.

TRANXENE tablets are contraindicated in patients with a known hypersensitivity to the drug and in those with acute narrow angle glaucoma.

Advise both patients and caregivers to consult with their physician before either increasing the dose or abruptly discontinuing TRANXENE, since benzodiazepines may cause psychological and physical dependence.

Withdrawal symptoms (similar in character to those noted with barbiturates and alcohol) have occurred following abrupt discontinuance of clorazepate. Withdrawal symptoms associated with the abrupt discontinuation of benzodiazepines have included convulsions, delirium, tremor, abdominal and muscle cramps, vomiting, sweating, nervousness, insomnia, irritability, diarrhea, and memory impairment. The more severe withdrawal symptoms have usually been limited to those patients who had received excessive doses over an extended period of time. Generally milder withdrawal symptoms have been reported following abrupt discontinuance of benzodiazepines taken continuously at therapeutic levels for several months. Consequently, after extended therapy,

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abrupt discontinuation of clorazepate should generally be avoided and a gradual dosage tapering schedule followed.
Antiepileptic drugs, including TRANXENE, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any antiepileptic drug for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Because of the lack of sufficient clinical experience, TRANXENE tablets are not recommended for use in patients less than 9 years of age.

The most frequently reported adverse reaction was drowsiness. Less commonly reported were: dizziness, various GI complaints (e.g. nausea, diarrhea, vomiting, dry mouth, abdominal discomfort, abdominal pain, dyspepsia, constipation and dysphagia), nervousness, blurred vision, dry mouth, headache and mental confusion. Other adverse reactions included insomnia, transient skin rashes, fatigue, ataxia, genitourinary complaints, irritability, diplopia, depression, lethargy, tremor, slurred speech, and fall. There have been reports of abnormal liver and kidney function tests and of decrease in hematocrit. Decrease in systolic blood pressure has been observed.

Prescribers or other health professionals should inform patients, their families, and their caregivers about the benefits and risks associated with treatment with clorazepate dipotassium and should counsel them in its appropriate use.

We are committed to helping address patients' unmet needs through our corporate mission. If you have questions or concerns regarding this product, please call Recordati Rare Diseases Medical Information at 1-888-575-8344.

Sandy S. Suh

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